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Docket No. GJE-89  
Serial No. 10/089,877Remarks

Claims 22-26, 28, 30, 32-35, 41, 43, 45, and 46 are pending in the subject application. Applicant gratefully acknowledges the Examiner's withdrawal of the objection and the previous rejections under 35 USC §§112, 102(b), 102(e), and 103(a). Applicant also gratefully acknowledges the Examiner's indication that claims 41, 43, 45, and 46 are free of the prior art. By this Amendment, Applicant has amended claims 22, 28, 30, 34, 41, 43, 45, and 46. Support for the amendments can be found throughout the subject specification and in the claims as originally filed. Claim 46, which referenced the solid support of claim 41, has been amended to recite all the elements and limitations of the solid support of claim 41. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 22-26, 28, 30, 32-35, 41, 43, 45, and 46 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

As an initial matter, Applicant would like to thank the Examiner for the courtesy of the telephonic conference conducted with Applicant's undersigned representative on December 15, 2004. Applicant respectfully submits that the amendments to the claims and the remarks presented herein are in accord with the substance of the telephonic conference in which the rejections under 35 USC §102 and §103 were discussed.

Claims 41, 43, 45, and 46 are rejected because of informalities. Specifically, the claims are objected to for using the abbreviation "FRET." In accordance with the Examiner's suggestion, claims 41, 43, and 46 have been amended to recite "fluorescence resonance energy transfer" with the abbreviation "FRET" in parentheses in claim 41. Accordingly, reconsideration and withdrawal of the objection, and an indication of allowance of the claims, is respectfully requested.

Claims 22-26, 28, 30, and 32-35 are rejected under 35 USC §112, second paragraph, as indefinite. Applicant respectfully asserts that the claims are definite. However, in regard to the rejection of claims 22-26, 28, 30, and 32-35 for the recitation of a "first" fluorescent molecule, Applicant has amended the claims to delete reference to "first" and to recite a "bound fluorescent molecule." This amendment is intended to clarify that the claimed method does not require multiple, distinct fluorescent molecules attached to the enzyme. However, it should be understood that the enzyme can also comprise, in addition to the "bound fluorescent molecule," a "bound label" as

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provided in dependent claims 28 and 30. The "bound label" is distinct from the "bound fluorescent molecule" of the claimed subject matter and this is clear from the disclosure in the subject specification. In regard to the rejection of claims 28, 30, and 34 for lack of antecedent basis, Applicant has amended those claims to recite a "bound" fluorescent molecule in accord with the language in claim 22. The amendments presented herein have been made to lend greater clarity to the claimed subject matter. Accordingly, reconsideration and withdrawal of the rejection under 35 USC §112, second paragraph, is respectfully requested.

Claims 22, 23, 25, 28, and 30 are rejected under 35 USC §102(c) as anticipated by Korlach *et al.* (Published U.S. Application 2003/0044781). In addition, claims 24, 26, 32, and 34 are rejected under 35 USC §103(a) as obvious over the Korlach *et al.* application in view of Chan *et al.* (U.S. Patent No. 6,210,896). Also, claim 33 is rejected under 35 USC §103(a) as obvious over Korlach *et al.* in view of Chan *et al.* (U.S. Patent No. 6,355,420) and claim 35 is rejected under 35 USC §103(a) as obvious over Korlach *et al.* in view of Ha *et al.* (1996). Applicant respectfully traverses each of these grounds of rejection.

Applicant respectfully asserts that the primary reference cited in each of the rejections, the Korlach *et al.* publication, does not teach or suggest the claimed invention. Moreover, the secondary references cited in the §103 obviousness rejections do not overcome the deficiencies or failings of the Korlach *et al.* reference and do not teach or suggest the elements of Applicant's claimed methods. The sequencing methods disclosed in the Korlach *et al.* publication all require the use of labeled nucleotides, whereas Applicant's claimed method does not require labeled nucleotides. In fact, in certain embodiments of Applicant's claimed methods, nucleotide monomers are not required at all (*e.g.*, where the polymerase is a helicase). Moreover, in Applicant's claimed method, the target polynucleotide is not labeled. In the methods disclosed in the Korlach *et al.* publication, labeled nucleotides are incorporated in the target polynucleotide for some period during enzyme processing (Applicant acknowledges that the Korlach *et al.* publication teaches that the label can be subsequently removed or cleaved from the nucleotide incorporated into the target polynucleotide). Thus, in the Korlach *et al.* methods, the target polynucleotide does comprise a label at some point or step during the method.

By this Amendment, Applicant has amended claim 22 to clarify that 1) individual nucleotide monomers, if utilized in the claimed method, are not labeled; and 2) that the target polynucleotide is not labeled prior to, during, or after enzyme processing along the target polynucleotide. Support for these amendments can be found throughout the subject specification and are implicit in the disclosure therein. It is well settled in patent law that the claim language of an amendment need not be disclosed word for word in a specification. *In re Wilder*, 222 USPQ 369, 372 (Fed. Cir. 1984) ("It is not necessary that the claimed subject matter be described identically, but the disclosure must convey to those skilled in the art that applicant had invented the subject matter later claimed.") (emphasis added). Applicant respectfully asserts that claim 22 already specifies that the target polynucleotide is not labeled during practice of the invention; however, the claim has been amended to clarify this aspect in accordance with the undersigned's telephonic conference with the Examiner.

The methods disclosed in the '896 Chan patent and the '420 Chan patent require a labeled polymer molecule, *i.e.*, a target polynucleotide, and the interaction between the labeled polymer and the labeled enzyme is detected. The method of the subject invention does not require a labeled polymer. Applicant's claimed invention requires only a simple measure of fluorescence of a single molecule in order to determine the sequence of a polynucleotide. There is no need for incorporated nucleotides to be labeled. A key requirement of the Chan patents is that a label must be present on the enzyme and a label must be present on the target polymer. As noted previously, Applicant's claimed method does not require that the target polynucleotide be labeled; claim 22 specifically recites that the target polynucleotide is not labeled. In addition, there is no teaching or suggestion in the Chan patents that the conformational change of an enzyme can be detected using only a fluorescent label on the enzyme, to determine the sequence of a target polymer.

Applicant maintains that the Ha *et al.* reference is even less relevant as it is not concerned with DNA sequencing procedures but is seeking to study protein folding. The general teaching of Ha *et al.* is that a fluorescent label can be used to monitor protein structure at single molecule resolution. The enzyme studied, staphylococcal nuclease, is used only as a model protein with no teaching or suggestion to apply this technique in the field of DNA sequencing.

In regard to the §102 rejection, as the Examiner is aware, in order to anticipate, a single reference must disclose within the four corners of the document each and every element and

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limitation contained in the rejected claim. *Scripps Clinic & Research Foundation v. Genentech Inc.*, 18 USPQ2d 1001, 1010 (Fed. Cir. 1991). In regard to the §103 rejections, as the Examiner is also aware, it is well established in patent law that in order to support a *prima facie* case of obviousness, a person of ordinary skill in the art must find both the suggestion of the claimed invention, and a reasonable expectation of success in making that invention, solely in light of the teachings of the prior art. *In re Dow Chemical Co.*, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988). Applicants respectfully asserts that the references cited in the Office Action, whether taken alone or in combination, do not teach or suggest each and every element of the claimed invention and do not provide the requisite expectation of success. Accordingly, reconsideration and withdrawal of the rejections under 35 USC §§102 and 103 is respectfully requested.

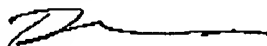
It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicant's agreement with or acquiescence in the Examiner's position.

In view of the foregoing remarks and amendments to the claims, Applicant believes that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicant invites the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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